



Getting Rid of Rotavirus

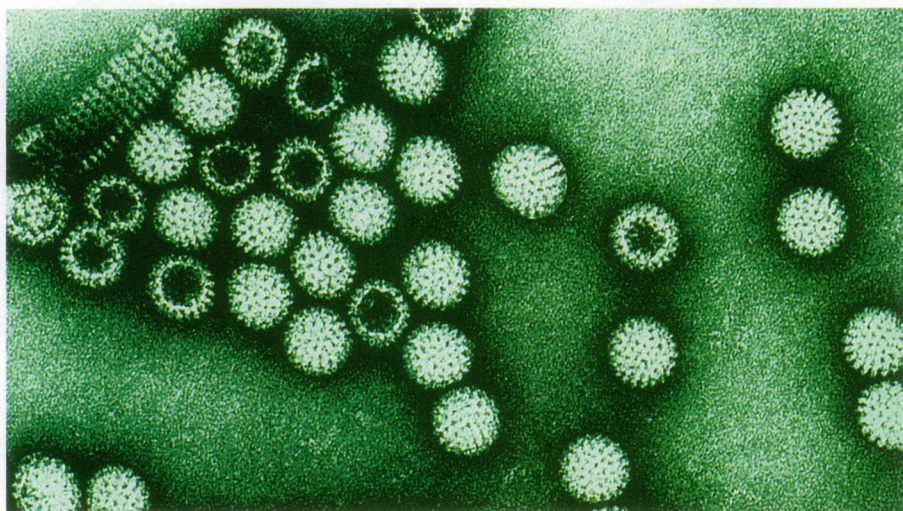
On 12 December 1997, the FDA's Vaccine and Related Biologicals Products Advisory Committee unanimously concluded that RotaShield, the first vaccine for rotavirus—a highly contagious disease that causes life-threatening diarrhea in young children—is safe and effective, and recommended licensing.

In the United States alone, rotavirus causes 3 million cases of childhood diarrhea, resulting in 500,000 doctor visits, 100,000 hospitalizations, and up to 100 deaths annually. Direct costs of the disease run to as much as \$400 million and indirect costs (such as lost work time for parents) total \$1.4 billion. Worldwide, rotavirus kills 873,000 children each year, largely in underdeveloped countries. The vaccine is intended to be administered in three doses at 2, 4, and 6 months of age when children receive their polio vaccine.

The RotaShield vaccine was created and patented by virologist and physician Albert Kapikian and his colleagues at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland. Kapikian, head of the epidemiology section of the Laboratory of Infectious Diseases, has devoted nearly 25 years to studying rotavirus. "It's exciting and gratifying as a physician to see that most babies can be protected from severe diarrhea with a product developed in our laboratory," he says.

Australian virologists discovered rotavirus in 1973. Later, several epidemiological studies proved that rotavirus was the most important agent involved in infantile diarrhea worldwide. Kapikian's ingenuity and perseverance helped overcome obstacles in creating the vaccine. For instance, human rotavirus resisted growth in cell cultures, whereas simian rotavirus grew well. The researchers worked to determine whether an animal rotavirus could protect humans, much in the same way that Edward Jenner determined 200 years ago that vaccinating people with cowpox could prevent smallpox. The final vaccine contains a weakened form of rotavirus obtained from rhesus monkeys, bioengineered with three genes from human rotavirus. This combination proved most effective at protecting people against the four most prevalent clinical strains of rotavirus.

The vaccine was tested successfully in numerous clinical trials. Among 2,000 infants in Venezuela, the vaccine reduced severe diarrheal illness by 88% and dehydration by 75%, and decreased hospitalizations



Charles Humphrey/CDC

Last of a dying breed? A new vaccine expected to be approved by the FDA may mean the end of rotavirus outbreaks.

by 70%. This study, reported in the 23 October 1997 issue of the *New England Journal of Medicine*, was the largest and most successful trial of the vaccine in a developing country. A multi-center trial conducted in the United States of 1,200 children showed that the vaccine protected 80% of the children against severe diarrhea and 100% against dehydration, as described in the January 1996 issue of *Pediatrics*. Another study, which appeared in the 25 October 1997 issue of *Lancet*, concluded that when tested on 2,400 Finnish children the vaccine reduced severe diarrhea by 91%, clinic visits for dehydration by 97%, and hospitalizations by 100%. In the latest study, published in the October 1997 issue of the *Journal of Pediatrics*, the vaccine prevented 69% of severe cases of diarrhea on American Indian reservations, where incidence rates of rotavirus disease run higher than for the general population. "The routine use of this vaccine could save lives and prevent illness," says Mathuram Santosham, director of the Johns Hopkins Center for American Indian and Alaskan Native Health in Baltimore, Maryland. In all clinical tests, the vaccine was safe and well-tolerated.

About 90% of all children are infected by rotavirus by age three regardless of hygienic conditions. Diarrhea is considered a normal part of childhood, and few hear about the small number of children who die yearly from rotavirus. Although a current television advertisement for a bathroom cleaner mentions that it kills rotavirus, in reality "parents in the U.S. don't know that rotavirus is a problem," says senior clinical

scientist Michael Pastorino of Wyeth-Ayerst Research in Radnor, Pennsylvania, a division of the company seeking licensure for the RotaShield vaccine. Both parents and physicians need to be educated about the new vaccine.

Wyeth-Ayerst is seeking a universal recommendation that all children be vaccinated for rotavirus from the Advisory Committee for Immunization Practices at the CDC, which sets the schedule of childhood immunizations.

Stockpiling Safety?

By spring, the Nuclear Regulatory Commission (NRC) is expected to act, once again, on the 15-year-old issue of whether it makes sense for states to consider stockpiling thousands of tablets of potassium iodide (KI) near nuclear power plants in case of an emergency. No one disputes that KI, a benign substance long approved for over-the-counter use, is an effective thyroid-blocking agent. And no one is arguing that the cost of KI is prohibitive. A 130-mg tablet costs \$.07; supplying all residents within five miles of one of the United States' 107 operating nuclear reactors would cost as little as \$200,000 (although distributing and disposing of the supply would add costs). Few even question the safety of the tablets. The issue is whether having KI on hand would make some residents trust their fate to a pill rather than to evacuation.

Many states, as well as the nuclear industry, believe evacuation should be the first line of protective action in a nuclear emergency.

KI isn't a "silver bullet," says Steve Unglesbee, a spokesman for the Nuclear Energy Institute in Washington, DC, because it can create a false sense of security as well as "ambiguity through choice." Unglesbee likes to quote an April 1997 Chicago Sun-Times editorial that argued against stockpiling: "The idea is akin to putting a dab of sunblock on your nose at the beach; you may end up with a protected brow, but the rest of your body will be scorched."

But supporters of stockpiling, including the American Thyroid Association, contend that it would be negligent of the industry and of state and federal governments not to endorse what they call a simple and cheap insurance policy. "I compare it to lifeboats and life jackets on a ferry," says Peter Crane, a staff attorney for the NRC and a long-time advocate for the tablets' use. "It's better to be evacuated in a lifeboat, but also helps to have on a life jacket."

The tablet works by saturating the thyroid with iodide, which the organ needs to make hormones needed by the nervous system and brain. A saturated thyroid will not, therefore, absorb cancer-promoting radioactive iodide that may escape into the air from a nuclear power plant's containment facility during a nuclear accident. Crane has been leading the effort to stockpile KI as a private citizen since 1989. He says his position comes from experience; Crane was diagnosed with thyroid cancer at age 26, more than 20 years after having his tonsils irradiated as a child in a Chicago hospital. He has battled the disease, which kills about 1,000 U.S. citizens annually, on and off for decades.

In 1989, when the NRC refused to change its opinion not to require KI stockpiling, Crane filed a professional opinion challenging that action. That was three years after the Chernobyl nuclear power plant accident, which resulted in about 900 cases

of thyroid cancer, leaving many Soviet children with the "Belarussian necklace," a surgical scar that goes from ear to ear, says Crane. But in Poland, upwind of the accident, children were given KI pills, and there has been no increase in thyroid cancer. Also, in 1989 the World Health Organization recommended preventive distribution of KI, and, to date, France and Switzerland have distributed it widely.

But with one-fourth of the world's reactors, the United States has taken a conservative attitude. Despite a federal recommendation following the Three Mile Island accident in 1979 to stockpile KI, the NRC did not endorse the recommendation in 1985, and deadlocked on the issue again in 1994 after Crane urged reconsideration. One survey considered by NRC commissioners showed that 33 of 43 responding states opposed stockpiling, in part because they would have to develop plans to distribute the pills.

Nevertheless, in October 1996 the federal government agreed to buy KI for any state that wanted it. Additionally, plans were made to stockpile KI in 27 metropolitan areas and three national stockpiles. To date, three city stockpiles exist but plans to move the medicine to accident sites do not.

Now Crane wants the NRC to change its language to say stockpiling is "reasonable and prudent" and that states should consider it. His petition was published in the Federal Register in December for public comment and is expected to be voted on by the NRC after February. Unglesbee says the industry will oppose the measure, as it always has. He says that requiring states to consider KI constitutes "an unfunded federal mandate" on states that have already decided that KI pills "work against more effective evacuation."

But not all states feel that way. Tennessee and Alabama already stockpile KI at emergency centers, and in December, Maine's radiation advisory committee recommended stockpiling. Their endorsement came after strong testimony that portions of the evacuation plan for the area surrounding the Maine Yankee nuclear reactor in Wiscasset, Maine, failed during a test. This reactor, the state's only nuclear plant, has since been closed.

Crane feels that the NRC will eventually endorse stockpiling. "It's a matter of people finding out about it just as

they did in Maine," he says. And what if the NRC votes his petition down? Well, he says, he can always ask for a judicial review.

Gamma Groceries

Highly publicized incidents last year, such as the recall by Hudson Foods, a Nebraska meat processor, of millions of pounds of hamburger contaminated with the potentially deadly bacteria *Escherichia coli* O157:H7, have made food safety a major concern in the United States. According to the Council for Agricultural Science and Technology, a nonprofit organization composed of 30 scientific societies, harmful bacteria carried in food can cause as many as 9,000 deaths annually.

In December, the FDA approved the use of ionizing radiation to kill harmful microorganisms in red meat as one more tool to protect the food supply. (The federal government had previously approved irradiation for poultry and fresh fruits and vegetables.) The move, which allows but does not require meat processors to irradiate meat, pleased food scientists and public health officials but worried some public interest and activist groups.

A prime irradiation target is ground beef, which can be laden with pathogens when contaminated carcasses are ground to make hamburger, says Michael Doyle, director of the Center for Food Safety and Quality Enhancement at the University of Georgia in Athens. Irradiating meat is a fairly simple process in which packaged meat is subjected to ionizing radiation—either gamma rays from radioactive materials such as cobalt 60 or cesium 137 or high energy electrons.

Though the U.S. Department of Agriculture has not drawn up rules to describe in detail how the process will work—it's estimated that rule development will take about a year—food scientists envision it occurring at the end of the packing process, just before the meat is shipped from the plant to retail stores. "It will make meat at the point of purchase at least 90% safer than it is today," says Curtis Melton, a professor of food science at the University of Tennessee in Knoxville.

Dennis Buege, a professor of animal science at the University of Wisconsin in Madison, says irradiation will increase ground beef's shelf life. "Rather than your package of ground beef staying in your refrigerator in good condition for three days, it may stay in good condition for six days," he says. Irradiation may also be particularly important in nursing homes and other institutional settings, where food safety is a major concern because food is prepared for relatively large numbers of people, says Buege.



Medical insurance? A current debate considers whether stockpiling potassium iodide near nuclear reactors offers a safeguard or a false sense of security.